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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,893	01/17/2001	Shih-Chieh Hung	11709-003001	6011

7590 11/17/2011

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
11/17/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/761,893	HUNG ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,4,6,9-20,34,35,38 and 43-45* is/are pending in the application.

5a) Of the above claim(s) *12-20 and 43-45* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,4,6,9-11,34,35 and 38* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *17 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 9/15/2011, in which claims 36, 37 and 42 were canceled. It is noted that the amendment is not compliant with 35 CFR 1.21(c). However, the amendment has been entered in the interest of compact prosecution. The markings of claim 1 have not been made relative to the previously entered version of the claim. In the amendment filed 9/15/2011 the phrase "and non-adherent cells on the upper plate" was deleted from step 1(c). Claims 4, 6, 9, 10, 11, 34, 35 were previously presented. Claims 1 and 38 have been amended. Claims 12-20 and 43-45 were previously withdrawn. Claims 1, 4, 6, 9-20, 34, 35, 38 and 43-45 are pending.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant elected Group I without traverse in the reply filed on 9/4/2001.

Claims 12-20 and 43-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/4/2001.

Currently, claims 1, 4, 6, 9-11, 34, 35 and 38 are under consideration.

Response to Arguments - Claim Objections

The objection of claim 42 is moot in view of Applicant's cancellation of the claims.

Response to Arguments - 35 USC § 112

The rejection of claims 36 and 37 under 35 U.S.C. 112, fourth paragraph, is moot in view of Applicant's cancellation of the claim in the reply filed 9/15/2011.

The rejection of claim 42 under 35 U.S.C. 112, first paragraph, is moot in view of Applicant's cancellation of the claim in the reply filed 9/15/2011.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 6, 9, 11, 34, 35 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Prockop et al (US Patent No. 7,374,937 B1, effective date March 14, 2000,

cited in a prior action; see the entire reference) and Matsui et al (US Patent No. 4,871,674, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 8/31/2011. The rejection statement has been rewritten to remove claims 36, 37 and 42, which were canceled in the reply filed 9/15/2011.

Caplan et al teach the isolation of human mesenchymal stem cells from aspirated marrow, comprising the steps of (i) applying the cells to a Percoll gradient and collecting the low density platelet fraction containing marrow-derived mesenchymal stem cells, platelet cells, and red blood cells; (ii) placing the cells in complete medium; (iii) allowing the cells to adhere to the surface of Petri dishes for one to seven days; and (iv) removing non-adherent cells after three days by replacing the original complete medium with fresh complete medium, thereby providing a homogenous population of human mesenchymal stem cells free of markers associated with hematopoietic cells (e.g., column 1, line 56 to column 3, line 19; column 11, line 63 to column 12, line 25). Caplan et al teach that complete medium and Dulbecco's modified Eagle's medium containing 10% fetal bovine serum and 1 g/L of glucose stimulates mesenchymal stem cell growth without differentiation and allows for the selective attachment of only mesenchymal stem cells to the plastic surfaces of the Petri dishes (e.g., column 8, line 45 to column 9, line 55; column 45, line 45 to column 46, line 34). Caplan et al teach that mesenchymal stem cells can be grown until the culture dishes become confluent (e.g., paragraph bridging columns 19-20). Caplan et al teach that when the culture dishes become confluent, the cells are detached with 0.25% trypsin with 0.1 mM EDTA for 10-15 minutes at 37° C, the action of trypsin is stopped with fetal bovine serum, the cells are counted, split 1:3 and replated in 7 ml of complete medium (e.g., paragraph bridging columns 19-20; paragraph bridging columns 40-41). Caplan et al teach

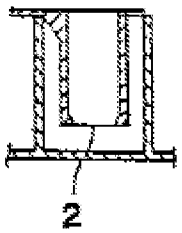
plating the recovered cells into 35 mm plates at 50,000 cells, which is a density of about 5 x $10^3/cm^2$ (e.g., column 41). Caplan et al teach that the mesenchymal stem cells can differentiate into bone, cartilage or adipose tissue (e.g., column 1, lines 40-52; column 47, lines 9-48). Moreover, Caplan et al teach that a porous filter can be used to remove red blood cells from the mesenchymal stem cells to provide an enriched population of mesenchymal stem cells (e.g., column 45, line 45 to column 46, line 34).

Caplan et al do not teach the method of isolating human mesenchymal stem cells where the mixed population of cells in medium is seeded into a culture device comprising an upper plate with pores and a lower plate base, where small cells pass through the pores in the upper plate and adhere to the lower plate.

Prockop et al teach that RS cells can be separated from non-RS mesenchymal stem cells by ultrafiltration. Prockop et al teach that smaller RS cells will pass through an ultrafiltration membrane having appropriately sized pores, and such a membrane is a Millipore brand 10 micrometer isopore polycarbonate (plastic) membrane (e.g., column 39, line 60 to column 40, line 42).

Matsui et al teach culturing cells in a cell culture device comprising a cell culture insert comprising a membrane filter (2) on the bottom of the culture cell, which is composed of polycarbonate (e.g., column 2, lines 41-55; column 3, lines 5-18). The culture device is shown in Figure 8, which is reproduced below:

Fig. 8



It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of isolating mesenchymal stem cells of Caplan et al to include the introduction of the mixed composition of cells comprising mesenchymal stem cells and medium into the culture dish taught by Matsui et al because Caplan et al teach that mesenchymal stem cells adhere to plastic for culturing, and Caplan et al teach it is within the ordinary skill in the art to use a filter to remove fat cells and red blood cells from cells of bone marrow. Furthermore, Prockop et al teach the collection of mesenchymal stem cells on a filter of polycarbonate containing 10 micrometer pores, and Matsui et al teach culturing cells in a device comprising a polycarbonate filter.

One would have been motivated to make such a modification in order to receive the expected benefit of providing an enriched population of mesenchymal stem cells without having to perform the extra steps of using a separate filter, or other separation method, as taught by Caplan et al, since red blood cell removal and mesenchymal stem cell culture could be performed simultaneously using the culture dish of Matsui et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Prockop et al (US Patent No. 7,374,937 B1, effective date March 14, 2000, cited in a prior action; see the entire reference) and Matsui et al (US Patent No. 4,871,674, cited in a prior action; see the entire reference) as applied to claims 1, 4, 6, 9, 11, 34, 35 and 38 above, and further in view of Pittenger et al (Science, Vol. 284, pages 143-147, 1999, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 8/31/2011. The rejection statement has been rewritten to remove claims 36, 37 and 42, which were canceled in the reply filed 9/15/2011.

The combined teachings of Caplan et al, Prockop et al, and Matsui et al are described above and applied as before.

Caplan et al, Prockop et al, and Matsui et al do not specifically teach that the mesenchymal stem cells are CD34-.

Pittenger et al teach the isolation of human mesenchymal cells from bone marrow taken from the iliac crest (e.g., page 143, right column). Pittenger et al teach that the mesenchymal stem cells are CD34- (e.g., paragraph bridging pages 143-144). The mesenchymal stem cells isolated by Pittenger et al are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically use a bone marrow aspirate from human iliac crest, because Caplan et al and Pittenger et al teach the use of bone marrow from iliac crest to isolate mesenchymal stem

cells that are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2). It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute iliac crest bone marrow for any other type of bone marrow to achieve the predictable result of recovering CD34- mesenchymal stem cells that are also capable of differentiating to adipose, cartilage or bone tissue.

Claims 1, 4, 6, 9, 11, 34, 35 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Burkitt et al (Wheater's Functional Histology (1993), page 60, cited in a prior action) and Mussi et al (US Patent No. 5,409,829, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 8/31/2011. The rejection statement has been rewritten to remove claims 36, 37 and 42, which were canceled in the reply filed 9/15/2011.

Caplan et al teach the isolation of human mesenchymal stem cells from aspirated marrow, comprising the steps of (i) applying the cells to a Percoll gradient and collecting the low density platelet fraction containing marrow-derived mesenchymal stem cells, platelet cells, and red blood cells; (ii) placing the cells in complete medium; (iii) allowing the cells to adhere to the surface of Petri dishes for one to seven days; and (iv) removing non-adherent cells after three days by replacing the original complete medium with fresh complete medium, thereby providing a homogenous population of human mesenchymal stem cells free of markers associated with hematopoietic cells (e.g., column 1, line 56 to column 3, line 19; column 11, line 63 to column 12, line 25). Caplan et al teach that complete medium and Dulbecco's modified Eagle's medium

containing 10% fetal bovine serum and 1 g/L of glucose stimulates mesenchymal stem cell growth without differentiation and allows for the selective attachment of only mesenchymal stem cells to the plastic surfaces of the Petri dishes (e.g., column 8, line 45 to column 9, line 55; column 45, line 45 to column 46, line 34). Caplan et al teach that mesenchymal stem cells can be grown until the culture dishes become confluent (e.g., paragraph bridging columns 19-20). Caplan et al teach that when the culture dishes become confluent, the cells are detached with 0.25% trypsin with 0.1 mM EDTA for 10-15 minutes at 37° C, the action of trypsin is stopped with fetal bovine serum, the cells are counted, split 1:3 and replated in 7 ml of complete medium (e.g., paragraph bridging columns 19-20; paragraph bridging columns 40-41). Caplan et al teach plating the recovered cells into 35 mm plates at 50,000 cells, which is a density of about 5 x $10^3/cm^2$ (e.g., column 41). Caplan et al teach that the mesenchymal stem cells can differentiate into bone, cartilage or adipose tissue (e.g., column 1, lines 40-52; column 47, lines 9-48). Moreover, Caplan et al teach that a porous filter can be used to remove red blood cells from the mesenchymal stem cells to provide an enriched population of mesenchymal stem cells (e.g., column 45, line 45 to column 46, line 34).

Caplan et al do not teach the method of isolating human mesenchymal stem cells where the mixed population of cells in medium is seeded into a culture device comprising an upper plate with pores and a lower plate base, where small cells pass through the pores in the upper plate and adhere to the lower plate.

Burkitt et al teach that red blood cells are 6.7-7.7 μm in diameter and nucleated cells have a diameter greater than 7.7 μm (page 60).

Mussi et al teach the introduction of a mixture of cells to be grown into a culture chamber in a suitable growth medium (e.g., column 2, lines 46-50). Mussi et al teach that the cells are grown in a culture insert contained within a well, where the insert is suspended in the well (e.g., paragraph bridging columns 3-4; Figure 4). The culture insert contains a membrane (20), which may be formed from a polymeric material such as polyethylene terephthalate, polycarbonate, and the like with open pores throughout (e.g., column 3, lines 50-53). Mussi et al teach that the pores are between about 0.2 to about 10 microns in diameter (e.g., column 3, lines 53-57).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of isolating mesenchymal stem cells of Caplan et al to include the introduction of the mixed composition of cells comprising mesenchymal stem cells in medium into the culture insert of the culture device of Mussi et al because Caplan et al teach it is within the ordinary skill in the art to use a filter to remove red blood cells from cells of bone marrow aspirate and Mussi et al teach the use of a porous polycarbonate filter membrane, where the pore diameter can be about 0.2 to about 10 microns in diameter, and Burkitt et al teach that red blood cells are the size which would pass through the filter of Mussi et al while nucleated mesenchymal stem cells of Caplan et al would be retained on top.

One would have been motivated to make such a modification in order to provide an enriched population of mesenchymal stem cells without the extra steps of using a column containing a filter, or other separation method, as taught by Caplan et al, since red blood cell removal and mesenchymal stem cell culture could be performed simultaneously using the culture dish of Mussi et al. Based upon the teachings of the cited references, the high skill of one of

ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Burkitt et al (Wheater's Functional Histology (1993), page 60, cited in a prior action) and Mussi et al (US Patent No. 5,409,829, cited in a prior action; see the entire reference) as applied to claims 1, 4, 6, 9, 11, 34, 35 and 38 above, and further in view of Pittenger et al (Science, Vol. 284, pages 143-147, 1999, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 8/31/2011. The rejection statement has been rewritten to remove claims 36, 37 and 42, which were canceled in the reply filed 9/15/2011.

The combined teachings of Caplan et al, Burkitt et al, and Matsui et al are described above and applied as before.

Caplan et al, Burkitt et al, and Matsui et al do not specifically teach that the mesenchymal stem cells are CD34-.

Pittenger et al teach the isolation of human mesenchymal cells from bone marrow taken from the iliac crest (e.g., page 143, right column). Pittenger et al teach that the mesenchymal stem cells are CD34- (e.g., paragraph bridging pages 143-144). The mesenchymal stem cells isolated by Pittenger et al are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically use a bone marrow aspirate from human iliac crest, because Caplan et

al and Pittenger et al teach the use of bone marrow from iliac crest to isolate mesenchymal stem cells that are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2). It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute iliac crest bone marrow for any other type of bone marrow to achieve the predictable result of recovering CD34- mesenchymal stem cells that are also capable of differentiating to adipose, cartilage or bone tissue.

Claims 1, 4, 6, 9, 11, 34, 35 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Guirguis (US Patent No. 5,077,012, cited in a prior action; see the entire reference) and Matsui et al (US Patent No. 4,871,674, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 8/31/2011. The rejection statement has been rewritten to remove claims 36, 37 and 42, which were canceled in the reply filed 9/15/2011.

Caplan et al teach the isolation of human mesenchymal stem cells from aspirated marrow, comprising the steps of (i) applying the cells to a Percoll gradient and collecting the low density platelet fraction containing marrow-derived mesenchymal stem cells, platelet cells, and red blood cells; (ii) placing the cells in complete medium; (iii) allowing the cells to adhere to the surface of Petri dishes for one to seven days; and (iv) removing non-adherent cells after three days by replacing the original complete medium with fresh complete medium, thereby providing a homogenous population of human mesenchymal stem cells free of markers associated with hematopoietic cells (e.g., column 1, line 56 to column 3, line 19; column 11, line 63 to column

12, line 25). Caplan et al teach that complete medium and Dulbecco's modified Eagle's medium containing 10% fetal bovine serum and 1 g/L of glucose stimulates mesenchymal stem cell growth without differentiation and allows for the selective attachment of only mesenchymal stem cells to the plastic surfaces of the Petri dishes (e.g., column 8, line 45 to column 9, line 55; column 45, line 45 to column 46, line 34). Caplan et al teach that mesenchymal stem cells can be grown until the culture dishes become confluent (e.g., paragraph bridging columns 19-20). Caplan et al teach that when the culture dishes become confluent, the cells are detached with 0.25% trypsin with 0.1 mM EDTA for 10-15 minutes at 37° C, the action of trypsin is stopped with fetal bovine serum, the cells are counted, split 1:3 and replated in 7 ml of complete medium (e.g., paragraph bridging columns 19-20; paragraph bridging columns 40-41). Caplan et al teach plating the recovered cells into 35 mm plates at 50,000 cells, which is a density of about 5 x $10^3/cm^2$ (e.g., column 41). Caplan et al teach that the mesenchymal stem cells can differentiate into bone, cartilage or adipose tissue (e.g., column 1, lines 40-52; column 47, lines 9-48). Moreover, Caplan et al teach that a porous filter can be used to remove red blood cells from the mesenchymal stem cells to provide an enriched population of mesenchymal stem cells (e.g., column 45, line 45 to column 46, line 34).

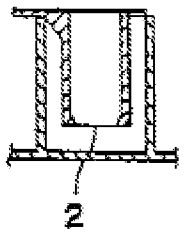
Caplan et al do not teach the method of isolating human mesenchymal stem cells where the mixed population of cells in medium is seeded into a culture device comprising an upper plate with pores and a lower plate base, where small cells pass through the pores in the upper plate and adhere to the lower plate.

Guirguis teaches the removal of red blood cells from a body fluid using a membrane with a smooth flat surface which is ideal for the collection of atypical cells from all types of body

fluids (e.g., column 3, lines 37-45; column 4). Guirguis et al teach that the membrane has a preferred pore size of 2 microns or less (e.g., column 4, lines 14-19). Guirguis teaches that the advantage of using a polycarbonate membrane is the minimum clogging by red blood cells and protein, well preserved cellular morphology with a high recovery rate, and excellent surface capture due to the pore structure and porosity (e.g., column 4, lines 43-64).

Matsui et al teach culturing cells in a cell culture device comprising a cell culture insert comprising a membrane filter (2) on the bottom of the culture cell, which is composed of polycarbonate (e.g., column 2, lines 41-55; column 3, lines 5-18). The culture device is shown in Figure 8, which is reproduced below:

Fig. 8



It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of isolating mesenchymal stem cells of Caplan et al to include the introduction of the mixed composition of cells comprising mesenchymal stem cells and medium into the culture dish taught by Matsui et al because Caplan et al teach it is within the ordinary skill in the art to culture mesenchymal stem cells on plastic and teach the use a filter to remove fat cells and red blood cells from cells of bone marrow. Furthermore, Guirguis teaches the use of a polycarbonate membrane for the removal of red blood cells from a body fluid, and Matsui et al teach culturing cells in a device comprising a polycarbonate filter.

One would have been motivated to make such a modification in order to receive the expected benefit of providing an enriched population of mesenchymal stem cells without having to perform the extra steps of using a separate filter as taught by Caplan et al, since red blood cell removal and mesenchymal stem cell culture could be performed simultaneously using the culture dish of Matsui et al. Further, one would have been motivated to use the polycarbonate (plastic) filter in place of the Leukosorb filter taught by Caplan et al, because Caplan et al teach that mesenchymal stem cells become selectively attached to plastic in DMEM containing 10% FBS and 1 g/L of glucose or complete medium, and Guirguis teaches that the advantage of using a polycarbonate membrane is the minimum clogging by red blood cells and protein, well preserved cellular morphology with a high recovery rate, and excellent surface capture due to the pore structure and porosity of the polycarbonate. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094, cited in a prior action; see the entire reference) in view of Guirguis (US Patent No. 5,077,012, cited in a prior action; see the entire reference) and Matsui et al (US Patent No. 4,871,674, cited in a prior action; see the entire reference) as applied to claims 1, 4, 6, 9, 11, 34, 35 and 38 above, and further in view of Pittenger et al (Science, Vol. 284, pages 143-147, 1999, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 8/31/2011. The rejection statement has been rewritten to remove claims 36, 37 and 42, which were canceled in the reply filed 9/15/2011.

The combined teachings of Caplan et al, Guirguis et al, and Matsui et al are described above and applied as before.

Caplan et al, Guirguis et al, and Matsui et al do not specifically teach that the mesenchymal stem cells are CD34-.

Pittenger et al teach the isolation of human mesenchymal cells from bone marrow taken from the iliac crest (e.g., page 143, right column). Pittenger et al teach that the mesenchymal stem cells are CD34- (e.g., paragraph bridging pages 143-144). The mesenchymal stem cells isolated by Pittenger et al are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to specifically use a bone marrow aspirate from human iliac crest, because Caplan et al and Pittenger et al teach the use of bone marrow from iliac crest to isolate mesenchymal stem cells that are capable of differentiating to adipose, cartilage or bone tissue (e.g., Figure 2). It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute iliac crest bone marrow for any other type of bone marrow to achieve the predictable result of recovering CD34- mesenchymal stem cells that are also capable of differentiating to adipose, cartilage or bone tissue.

Response to Arguments - 35 USC § 103

The rejection of claims 36, 37 and 42 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Prockop et al and Matsui et al is moot in view of Applicant's cancellation of the claims in the reply filed 9/15/2011.

The rejection of claims 36, 37 and 42 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Burkitt et al and Mussi et al is moot in view of Applicant's cancellation of the claims in the reply filed 9/15/2011.

The rejection of claims 36, 37 and 42 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Guirguis and Matsui et al is moot in view of Applicant's cancellation of the claims.

With respect to the rejection of claims 1, 4, 6, 9, 11, 34, 35 and 38 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Prockop et al and Matsui et al; the rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Prockop et al and Matsui et al, and further in view of Pittenger et al; the rejection of claims 1, 4, 6, 9, 11, 34, 35 and 38 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Burkitt et al and Mussi et al; the rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Burkitt et al and Mussi et al, and further in view of Pittenger et al; the rejection of claims 1, 4, 6, 9, 11, 34, 35 and 38 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Guirguis and Matsui et al; and the rejection of claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Guirguis and Matsui et al, and further in view of Pittenger et al, Applicant's arguments filed 9/15/2011 have been fully considered but they are not persuasive.

The response asserts that the "purifying" limitation recited in claim 1 was not taught in the prior art.

This argument is not found persuasive. Claim 1, step (c) recites "purifying mesenchymal stem cells by removal of hematopoietic stem cells." Caplan et al teach removing non-adherent

cells after three days of culture by replacing the original complete medium with fresh complete medium, thereby providing a homogenous population of human mesenchymal stem cells free of markers associated with hematopoietic cells (e.g., column 1, line 56 to column 3, line 19; column 11, line 63 to column 12, line 25).

The response notes that the Matsui patent (US Patent No. 4,871,674) issued on 10/3/1989; the Caplan patent (US Patent No. 5,811,094) issued on 9/22/1998; and the Prockop patent has an actual filing date of 10/25/2000 (and an effective filing date of 3/14/2000). The response notes that the present application was filed on 1/17/2001 and claims foreign priority to Taiwan 89121676, which was filed 10/17/2000. Thus, the response asserts that the time frame does not support the assertion that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine these three prior arts and do some modifications. The response asserts that if it had been obvious, Prockop would have combined the teachings of Matsui and Caplan to reach the presently claimed method. Applicant would like to know how it would be obvious to one of ordinary skill in the art and how one would have a reasonable expectation of success.

These arguments are not found persuasive. First, it is noted that all of the cited reference are prior-art. Second, in response to applicant's argument based upon the age and content of the references, contentions that the Prockop patent does not disclose the claimed invention in its entirety is not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. Third, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of isolating mesenchymal stem cells of Caplan et al to include the introduction of the mixed

composition of cells comprising mesenchymal stem cells and medium into the culture dish taught by Matsui et al because Caplan et al teach that mesenchymal stem cells adhere to plastic for culturing, and Caplan et al teach it is within the ordinary skill in the art to use a filter to remove fat cells and red blood cells from cells of bone marrow. Furthermore, Prockop et al teach the collection of mesenchymal stem cells on a filter of polycarbonate containing 10 micrometer pores, and Matsui et al teach culturing cells in a device comprising a polycarbonate filter. Given these specific teachings in the prior art references, one would have an expectation of success in adhering mesenchymal stem cells to a polycarbonate filter containing 10 micrometer pores, and purifying the mesenchymal stem cells by removing non-adherent hematopoietic cells and other non-mesenchymal cells. The combined teachings of the references rely upon a known property of selective adherence of mesenchymal stem cells. See the Caplan patent. Furthermore, the following rejections do not rely upon the teachings of the Prockop patent: the rejection of claims 1, 4, 6, 9, 11, 34, 35 and 38 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Burkitt et al and Mussi et al; the rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Burkitt et al and Mussi et al, and further in view of Pittenger et al; the rejection of claims 1, 4, 6, 9, 11, 34, 35 and 38 under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Guirguis and Matsui et al; and the rejection of claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al in view of Guirguis and Matsui et al, and further in view of Pittenger et al.

The arguments presented at paragraph 4 of the reply are directed to withdrawn claims 43-45 and thus are not relevant to the rejections of record. Thus, the arguments presented at paragraph 4 are not persuasive.

For these reasons, and the reasons made of record in the previous office actions, the rejections are maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is (571)272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Dunston/
Primary Examiner
Art Unit 1636